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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,974	01/27/2000	Connie S. Schmaljohn	003/115/SAP RIID96-10	9304

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Attn MCMR JA Elizabeth Arwine Patent Atty
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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	26

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/491,974	SCHMALJOHN ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communicati n appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *28-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *46 and 47* is/are allowed.

6)☐ Claim(s) *28-32,35-41,44,45,48 and 49* is/are rejected.

7)☐ Claim(s) *33,34,42,43,50 and 51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on June 30, 2003, paper number 23, has been entered.

DETAILED ACTION

This application filed January 27, 2000, claims benefit of provisional application 60/117,680, filed January 29, 1999.

Applicants' amendment filed June 30, 2003, paper number 25, has been received and entered. Claim 28 has been amended. Claims 28-51 are pending and currently under examination.

Response to Amendment

The declaration of Jay Hooper filed under 37 CFR 1.132 filed June 30, 2003, paper number 24, is insufficient to overcome the rejection of claims 28-32, 35-41, 44, 45, 48 and 49 based upon 35 USC 103 as set forth in the last Office action because: it is unclear from the data

presented in the declaration that demonstrates the unexpected results of administering and expressing both G1 and G2 glycoprotein of a hantavirus M gene is commensurate in scope with the instant claims. More specifically, claim 28 encompasses a composition comprising (a) an inert particle coated with a polynucleotide, and (b) the polynucleotide on said particle wherein said polynucleotide comprises a promoter operatively linked to a hantavirus M gene encoding both a G1 glycoprotein and G2 glycoprotein, however from the experiments detailed in the declaration, it is not clear how the immunization was done or if the immunization was done with the instantly claimed composition. Examiner would agree that the results presented in the declaration clearly indicate that administration and expression of both G1 and G2 glycoproteins of a hantavirus M gene are required to provide protective immunity to hantavirus. Furthermore, Examiner would note that the experiments demonstrate that the protective immunity provided by the expression of both G1 and G2 glycoproteins of one specific hantavirus M gene extends protective immunity beyond the one specific hantavirus represented by the G1 and G2 glycoprotein sequences of the hantavirus M gene expressed as exemplified in Table 2 of the declaration (page 3 of declaration). However, while the details of the experiments indicate that expression of both G1 and G2 glycoproteins of a hantavirus M gene have the unexpected result of providing protective immunity, the results do to clearly indicate that this unexpected result extends to compositions wherein the polynucleotide is coated onto inert particles for administration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-32, 35-42, 44, 45 and 49 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schmaljohn (Rev. Med. Virol., 4:185-196, 1994), Chu *et al.* (J. Virol., 69(10):6417-6423, 10/95), Montgomery *et al.* (Pharmacol. Ther., 74(2):195-205, 1997), Donnelly *et al.* (Ann. Rev. Immunol., 15:617-648, 1997), and Arikawa *et al.* (Virol., 176:114-125, 1990).

Applicants note the amendments to the claims and the evidence provided in the declaration of Jay Hooper (paper number 24). Applicants argue that given the specific teachings of each of the references one would not have been motivated to combine the cited references nor would have had an expectation of success that the resulting composition resulted in an effective vaccine. In particular, noting that amended claim 28 requires expression of G1 and G2 glycoproteins of a hantavirus M gene, and that the experimental results of the declaration clearly indicate that providing expression of only one of G1 or G2 glycoproteins of a hantavirus M gene fails to provide protective immunity, Applicants argue that the instant claims are drawn to an invention which would have not have been expected in light of the combined teachings of

Schmaljohn, Chu *et al.*, Montgomery *et al.*, Donnelly *et al.*, and Arikawa *et al.* See Applicants' amendment, pages 3-4. Applicants' arguments have been fully considered, but not found persuasive.

As noted above in response the declaration of Jay Hooper, Examiner agrees that the results presented in the declaration indicate that administration and expression of both G1 and G2 glycoproteins of a hantavirus M gene are required to provide protective immunity to hantavirus and that the experiments demonstrate that the protective immunity provided by the expression of both G1 and G2 glycoproteins of one specific hantavirus M gene extends protective immunity beyond the one specific hantavirus represented by the G1 and G2 glycoprotein sequences of the hantavirus M gene expressed. However, the details of the experiments indicate that expression of both G1 and G2 glycoproteins of a hantavirus M gene have the unexpected result of providing protective immunity, the evidence of record does not indicate that this unexpected result extends to compositions wherein the polynucleotide is coated onto inert particles for administration as instantly claimed.

As set forth in the previous office action, Montgomery *et al.* reviews the state of the DNA vaccine art and teaches that "[i]f known antigens elicit protective antibodies from a natural infection, results in many disease models support the hypothesis that expression of the antigen from a plasmid will elicit a similar response" (page 198, left column). To the same extent, Donnelly *et al.* reviews the state of the DNA vaccine art and teaches DNA vaccines offer a simple alternative to other methods involving e.g. live attenuated vaccinia virus recombinants

which "may be restricted in use due to concerns about their safety" (page 619). Donnelly further draw attention to the "remarkable number of publications demonstrating efficacy of DNA vaccines in various preclinical models that have appeared since the publication of the initial demonstration of the generation of protective efficacy attest to the simplicity as well as the robustness of the technology" (page 620) and discusses the advantage and simplicity associated with being able to alter constructs or mixing different plasmid to explore the use of different forms of an antigen (see for example page. 625). It is noted that Applicants do not argue that the each of the specific embodiments instantly claimed are not set forth, rather that the references would not be combined with any expectation of success. However, each of the cited references are within the art of vaccines. One of skill in the art would be apprised of the various means to make and use a vaccine composition. Clearly, Schmaljohn, Chu *et al.* and Arikawa *et al.* provide evidence and motivation for a vaccine comprising the hantavirus proteins encompassed by the claims. Further, in the art of vaccines, DNA vaccines were generally known and demonstrated to be effective for known antigens. As set forth previously, given the differences between a vaccinia virus vaccine and DNA vaccine one of ordinary skill in the art would have been further motivated to combine these teachings in view of the advantages of DNA vaccines over live vaccinia virus vaccines since DNA vaccines are predicted to be safer, easier to maintain, less expensive, and offering greater flexibility, including protection against multiple antigens and/or pathogens as specifically suggested by Donnelly and Montgomery *et al.*

The composition and the method of use are broadly drawn to any polynucleotide operative in a mammalian cell and does not exclude the use of any particular vector as long as it is functional in a mammalian cell. The hantaan virus proteins G1 and G2 encoded by the M gene were known and demonstrated to serve as effective antigens in a vaccine composition as demonstrated by Schmaljohn, Chu *et al.* and as proposed by Arikawa *et al.* Further, the antigens can be generated and provided by a variety of polynucleotide vectors. Clearly, the prior art of record teaches that there is an expectation that these particular hantavirus proteins would serve as antigens in a vaccine when administered to a subject. In summary, the antigens encompassed by the instant claims were known, used and shown to be effective in vaccine compositions and in light of the teachings of Montgomery and Donnelly, there would have been a reasonable expectation of success to formulate these antigens in the form of a DNA vaccine. While the data provided in the declaration provides evidence that expression of only one glycoprotein either G1 or G2 of the M gene with the specific vectors set forth in the examples provides an unexpected result for expressing both using the pWRG vector, the evidence does not specifically support that this would be extended to other vectors and/or any other promoter sequence for expression, nor does it specifically support that the unexpected result extends to a composition comprising a polynucleotide coated unto an inert particle as instantly claimed. Further clarification of the details of the experiments set forth in the declaration commensurate in scope with claims would be considered and may obviate the basis of the rejection.

Thus, for the reasons above and of record, the claimed invention as a whole was clearly *prima facie* obvious, and therefore the rejection is maintained.

Conclusion

As noted in the previous office action, claim 46 and 47 are allowed. Claims 33, 34, 42, 43, 50 and 51 are objected to because they depend on rejected claims, however would be found allowable if rewritten in independent form encompassing all the limitations of the independent claim and any intervening claims. Specifically, the claims directed to SEQ ID NO: 1 and the specific construct set forth in SEQ ID NO: 3 are free of the art of record because the antigenic determinants comprised by these specific sequences have not been previously disclosed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

Joe Woitach
AU1632